Figure 1

(a) MCF-7 cells

(b) T47D cells

Co-IP

PR RIME

ERα RIME

PR-Chaperone complex

Co-factors

T47D cells

MCF-7 cells

T-47D cells

MCF-7 cells

Co-IP

IP: ERα

IP: ERα

Prog: - +

- +

T47D cells

MCF-7 cells

IP: ERα

IP: ERα

Prog: - +

- +

PR-B

PR-A

Co-factors

FoxA1

ER

PR

HSP90B

FKBP5

FKBP4

PR-Chaperone complex

+ progesterone

OR

Co-factors

FoxA1

ER

PR
Figure 2

(a) Genes ranked by RNA-seq log2 FC

(b) ChIP-seq

<table>
<thead>
<tr>
<th>Progesterone</th>
<th>ERα</th>
<th>PR</th>
<th>p300</th>
</tr>
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<tbody>
<tr>
<td>-</td>
<td></td>
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<td>-</td>
</tr>
<tr>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
</tr>
</tbody>
</table>

(c) T-47D cells: Binding overlap

(d) GSEA analysis (ERα binding and gene expression)
Figure 3

(a) Control, E2, E2 + Prog

(b) Xenograft tumours

Day 25
7.8 x 10^9

8.57 x 10^7
(p/sec/cm^2/sr)

(c) ERα ChIP-seq: xenografts

(3,603 differential ERα binding events)

Log concentration

Decreased with E2 + P
Increased with E2 + P

(d) Ex vivo tumours: % Ki67 changes

E2 + Control
E2 + Prog
E2 + Tam
E2 + Tam + Prog

p = 0.02

(e) Ex vivo tumours: Ki67 expression

(f) MCF-7 xenografts

Normalised tumour volume

Time (days)
**Figure 4**

**a** ERα negative vs ERα positive

<table>
<thead>
<tr>
<th>Copy number status</th>
<th>Number</th>
<th>% of subtype</th>
<th>Number</th>
<th>% of subtype</th>
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<tbody>
<tr>
<td>Deletion</td>
<td>31</td>
<td>7.1</td>
<td>314</td>
<td>21</td>
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<tr>
<td>Neutral</td>
<td>381</td>
<td>86.8</td>
<td>1094</td>
<td>73</td>
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<tr>
<td>Gain</td>
<td>20</td>
<td>4.6</td>
<td>54</td>
<td>3.6</td>
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<tr>
<td>Amplification</td>
<td>7</td>
<td>1.6</td>
<td>36</td>
<td>2.4</td>
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<tr>
<td>Total</td>
<td>439</td>
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<td>1498</td>
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</table>

**b** mRNA and CNA (in ERα+ disease)

<table>
<thead>
<tr>
<th>Expression</th>
<th>Deletion</th>
<th>Neutral</th>
<th>Gain</th>
<th>Amplification</th>
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<td>10</td>
<td>9</td>
<td>8</td>
<td>7</td>
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<tr>
<td></td>
<td>6</td>
<td>5</td>
<td>4</td>
<td>3</td>
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<tr>
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<td>2</td>
<td>1</td>
<td>0</td>
<td>-1</td>
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</table>

*p < 0.001*

**c** ERα+ breast cancer (1,484 cases)

Breast cancer specific survival

- *P* = 0.001
- *P* - value = 0.001

**d** ERα mRNA levels (Luminal B cases)

<table>
<thead>
<tr>
<th>ERα expression</th>
<th>Loss</th>
<th>Neutral/gain</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Deletion</td>
<td>Neutral</td>
</tr>
<tr>
<td></td>
<td>Gain</td>
<td>Amplification</td>
</tr>
</tbody>
</table>

*p < 0.001*

**e** Fold change (in tumours)

- *P*-induced
- *P*-repressed

| PGR loss       | Deletion   | Neutral      |
| PGR neutral/gain | Gain       | Amplification|

*p < 0.001*

**f** Frequency of PgR CNA by subtype (PAM50)

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Basal</th>
<th>HER2</th>
<th>Luminal A</th>
<th>Luminal B</th>
<th>Normal</th>
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<tbody>
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<tr>
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<td>0.0</td>
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</table>

**g** Frequency of PgR CNA by subtype (Integrative cluster)

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<th>Frequency</th>
<th>Integrand cluster</th>
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<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
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<tbody>
<tr>
<td></td>
<td>ERα expression (%)</td>
<td>88.5</td>
<td>95.8</td>
<td>95.9</td>
<td>69.4</td>
<td>41.6</td>
<td>100</td>
<td>98.4</td>
<td>99.3</td>
<td>85.6</td>
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<td>PR expression (%)</td>
<td>43.2</td>
<td>70.8</td>
<td>72.8</td>
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<td>45.9</td>
<td>78.9</td>
<td>78.9</td>
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<td>HER2 expression (%)</td>
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<td>0.3</td>
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**Prognosis**

- Good
- Intermediate
- Poor